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**UTILITY PATENT APPLICATION TRANSMITTAL LETTER
AND FEE TRANSMITTAL FORM (37 CFR 1.53(b))**

BOX PATENT APPLICATION

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Transmitted herewith for filing under 37 CFR 1.53(b) is:

- ☒ a patent application
☐ a Continuation ☐ a Divisional ☐ a Continuation-in-Part (CIP)
of prior application no.: ; filed
☐ A Small Entity Statement(s) was filed in the prior application; Status still proper and desired.

Inventor(s) or Application Identifier:

**David W. Barry, Carolyn S. Underwood, Bruce J. McCreedy,
David D. Hadden and Jason L. Lucas**

Entitled: **SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING
THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS**

Enclosed are:

1. ☒ Application Transmittal Letter and Fee Transmittal Form (*A duplicate is enclosed for fee processing*)
2. ☒ **55** pages of Specification (including **69** claims)
3. ☒ **21** sheets of Drawings (35 USC 113)
4. ☒ Oath or Declaration
 - a. ☒ newly executed (*original or copy*)
 - b. ☐ copy from prior application (37 CFR 1.63(d) (*for continuation/divisional*) [Note Box 5 Below]
 - c. ☐ **DELETION OF INVENTOR(S)** (*Signed statement deleting inventor(s) named in the prior application*)
5. ☐ Incorporation By Reference (*useable if box 4b is checked*)

The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.
6. ☐ Microfiche Computer Program (*Appendix*)
7. ☒ Assignment papers (2) (*cover sheet(s) and document(s)*)
8. ☒ Small Entity Statement(s)
9. ☒ Information Disclosure Statement, PTO-1449, and **8** references cited
10. ☐ Preliminary Amendment (*Please enter all claim amendments prior to calculating the filing fee.*)
11. ☐ English Translation Document
12. ☐ Certified Copy of Application No. ; Filed

13. ☐ Sequence Listing/ Sequence Listing Diskette
 a. ☐ computer readable copy
 b. ☐ paper copy
 c. ☐ statement in support
 14. ☐ An Associate Power of Attorney
 15. ☒ Return Receipt Postcard (MPEP 503) *(Should be specifically itemized)*
 16. ☐ Other:

The fee has been calculated as shown below:

	Column 1 No. Filed	Column 2 No. Extra	Small Entity Rate Fee	Large Entity Rate Fee
BASIC FEE			\$380.00	\$760.00
TOTAL CLAIMS	69 - 20 =	49	x 09 = \$ 441.00	x 18 = \$
INDEP CLAIMS	3 - 3 =	0	x 39 = \$ 0	x 78 = \$
<input type="checkbox"/> MULTIPLE Dependent Claims Presented			+ 135 = \$	+ 270 = \$
<i>If the difference in Col. 1 is less than zero, Enter "0" in Col. 2</i>			Total \$ 821.00	Total \$

- ☐ A check in the amount of \$ to cover the filing fee is enclosed.
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- ☒ The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to Deposit Account No. 50-0220.
- ☒ Any additional filing fees required under 37 CFR 1.16.
- ☒ Any patent application processing fees under 37 CFR 1.17.

Respectfully submitted,

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney's Docket No. 9045-2

Applicant or Patentee: David W. Barry et al.

Serial No. or Patent No.: To be assigned

Filed or Issued: Concurrently herewith

Title: **SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR
GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS**

VERIFIED STATEMENT CLAIMING SMALL ENTITY STATUS
(37 C.F.R. § 1.9(f) & 1.27(c))--SMALL BUSINESS CONCERN

I hereby declare that I am

☐

the owner of the small business concern identified below:

☒

an official of the small business concern empowered to act
on behalf of the concern identified below:

NAME OF SMALL BUSINESS CONCERN: Triangle Pharmaceuticals, Inc.
ADDRESS OF SMALL BUSINESS CONCERN: 4 University Place
4611 University Drive
Durham, North Carolina 27707

I hereby declare that the above-identified small business concern qualifies as a small business concern as defined in 13 C.F.R. § 121.1301-1305, and reproduced in 37 C.F.R. § 1.9(d), for purposes of paying reduced fees to the United States Patent and Trademark Office, under Section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time, or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention described in:

☒

the specification filed herewith with title as listed above.

☐

the application identified above.

☐

the patent identified above.

If the rights held by the above-identified small business concern are not exclusive, each individual, concern, or organization having rights in the invention must file separate verified statements averring to their status as small entities, and no rights to the invention are held by any person, other than the inventor, who would not qualify as an independent

inventor under 37 C.F.R. 1.9(c) if that person made the invention, or by any concern which would not qualify as a small business concern under 37 C.F.R. § 1.9(d), or a nonprofit organization under 37 C.F.R. § 1.9(e).

Each person, concern, or organization having any rights in the invention is listed below:

- ☒ no such person, concern, or organization exists.
☐ each such person, concern, or organization is listed below.

Name: _____

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Separate verified statements are required from each named person, concern, or organization having rights to the invention averring to their status as small entities. (37 C.F.R. § 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 C.F.R. § 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: David W. Barry, M.D.

TITLE OF PERSON OTHER THAN OWNER: Chairman and Chief Executive Officer

ADDRESS OF PERSON SIGNING: 1810 South Lakeshore Drive, Chapel Hill, North Carolina 27514

SIGNATURE: David W. Barry

DATE: April 1, 1999

SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR
GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS

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Related Applications

10 This application claims the benefit of U.S. Provisional Application No. 60/080,629 filed April 3, 1998.

Field of the Invention

15 This invention concerns systems, methods and computer program products for guiding the selection of therapeutic treatment regimens for complex disorders such as cancer and HIV-1 infection, wherein a ranking of available treatment regimens is generated and
20 advisory information clinically useful for treating patients is provided.

Background of the Invention

Therapeutic treatment regimens for disorders such as HIV-1 infection (acquired immune deficiency syndrome or AIDS) and cancer are increasingly complex.

5 New data and new therapeutic treatment regimens continue to modify the treatments available, and it is difficult for all but the specialist to remain current on the latest treatment information. Further, even those who are current on the latest treatment
10 information require time to assimilate that information and understand how it relates to other treatment information in order to provide the best available treatment for a patient. Combination therapeutic treatment regimens exacerbate this problem by making
15 potential drug interactions even more complex. Finally, an increasingly sophisticated patient population, in the face of a vast volume of consumer information on the treatment of disease, makes the mere statement of a treatment regime, without explanation, difficult for
20 the patient to accept.

R. Miller et al., *Summary Recommendations for Responsible Monitoring and Regulation of Clinical Software Systems*, Ann. Intern. Med. **127**, 842-845 (1997), describes policy guidelines indicating the
25 desirability of systems that generate advice for clinician users in a manner that users can easily override. Solutions to this need are neither suggested nor disclosed.

M. Pazzani et al., *Application of an Expert System in the Management of HIV-Infected Patients*, J. Acquired Immune Deficiency Syndromes and Human
30

66T040 202E8360
Retrovirology **15**, 356-362 (1997) (accepted May 12, 1997), describes a rule-based expert system by which protease, reverse transcriptase, and integrase segments of HIV are cloned and entered into an expert system that recommends two, three, and four drug regimens. A means for easily overriding the advice given is neither suggested nor disclosed.

U.S. Patent No. 5,672,154 to Sillen describes a method for giving patients individualized, situation-dependent medication advice. The recommended type of medicine may include at least two different medicines. No means for ranking multiple treatment options is disclosed, and no means for explaining why treatment options were rejected is given. Rather, this system is primarily concerned with generating new rules from patient information to optimize a particular therapy for diseases such as Parkinson's disease, epilepsy and abnormal blood pressure.

U.S. Patent No. 5,694,950 to McMichael describes a method and system for use in treating a patient with immunosuppressants such as cyclosporin. An expert system is employed to generate a recommendation on whether the immunosuppressant dosage should be changed and, if so, how. Ranking or selection among a plurality of different combination therapeutic treatment regimens is not suggested.

U.S. Patent No. 5,594,638 to Iliff describes a medical diagnostic system that provides medical advice to the general public over a telephone network. This system is not concerned with generating a recommendation for a combination therapeutic treatment

regimen for a known disease (see also U.S. Patent No. 5,660,176 to Iliff).

Summary of the Invention

5 In view of the foregoing, an object of the invention is to provide systems, methods and computer program products for selecting therapeutic treatment regimens for patients in which available treatments are listed, and optionally ranked, while unavailable or
10 rejected treatment regimens (e.g., regimens that would not be effective, or would be dangerous) are not displayed or are assigned a low rank and are indicated to a user as not likely to be efficacious, or not preferred due to patient-specific complicating factors
15 such as drug interaction from concomitant medications.

 A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the available treatment options can be readily understood.

20 A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the implications of selecting a particular treatment regimen can be readily understood.

25 A further object of the invention is to provide systems, methods and computer program products for selecting treatment regimens in which the reasons for rejection of a particular regimen can be readily understood.

30 A still further object of the invention is to provide systems, methods and computer program products

for obtaining information about the efficacy of previous treatment regimens imposed on patients.

A method of the present invention includes providing patient information to a computing device that includes various knowledge bases. For example, a first knowledge base may include a plurality of different therapeutic treatment regimens for a disease or medical condition. A second knowledge base may include a plurality of expert rules for selecting a therapeutic treatment regimen for the disease or medical condition. A third knowledge base may include advisory information useful for the treatment of a patient with different constituents of different therapeutic treatment regimens. A fourth knowledge base may include information about past therapies, such as how a patient has fared under previous therapies.

A listing (preferably a ranked listing) of therapeutic treatment regimens for a patient is generated in the computing device. Advisory information for one or more treatment regimens in the listing is generated in the computing device based on the patient information and the expert rules.

In a preferred embodiment, the method described above further includes entering a user-defined therapeutic treatment regimen for the disease (or medical condition) that may not be displayed from the system knowledge base-generated therapeutic treatment regimens, and generating in the computing device advisory information for the user-defined combination therapeutic treatment regimen.

In addition, in a preferred embodiment, the

method described above further includes entering a rejected therapeutic treatment regimen for the disease (or medical condition) that is included in the first knowledge base but not recommended from the ranking (or given a very low ranking), and generating in the computing device advisory information for the non-recommended/low ranked therapeutic treatment regimen, wherein the advisory information includes at least one reason for not recommending (or low ranking) the therapeutic treatment regimen.

Further objects and aspects of the present invention are explained in detail in the drawings herein and the specification set forth below.

Brief Description of the Drawings

The accompanying drawings, which are incorporated in and constitute a part of the specification, illustrate embodiments of the invention and, together with the description, serve to explain principles of the invention.

Fig. 1 illustrates a process of the instant invention, including routines for entering a user-defined therapeutic treatment regimen and for entering a "non-recommended" therapeutic treatment regimen.

Fig. 2 schematically illustrates a system or apparatus of the present invention.

Fig. 3 illustrates a client-server environment within which the system of **Fig. 2** may operate, according to an embodiment of the present invention, and wherein a central server is accessible by at least one local server via a computer network,

such as the Internet, and wherein each local server is accessible by at least one client.

Fig. 4 illustrates a medical history user interface for entering data about a patient's medical history according to the present invention.

Fig. 5 illustrate a user interface chart for monitoring a patient's condition during a particular therapeutic treatment regimen over a period of time according to the present invention.

Fig. 6 illustrates a therapy evaluation user interface that facilitates evaluation of various therapeutic treatment regimen options with respect to relative efficacy, individualized adjusted relative efficacy, dosage, frequency, cost, medical complications and drug interactions according to the present invention.

Fig. 7 illustrates various symbols for providing information about a therapeutic treatment regimen option within the therapy list box of the therapy evaluation user interface of **Fig. 6** according to the present invention.

Fig. 8 illustrates the therapy details box of **Fig. 6** in "full screen" mode.

Fig. 9 illustrates a pop-up menu including an indexed electronic link to a PDR® that can be activated from within the therapy list box of the therapy evaluation user interface of **Fig. 6** according to the present invention.

Figs. 10A-10D illustrate various functions of the present invention as described in Example 1.

Figs. 11A-11E illustrate various functions of

the present invention as described in Example 2.

Figs. 12A-12C illustrate various functions of the present invention as described in Example 3.

5

Detailed Description of the Invention

The present invention now will be described more fully hereinafter with reference to the accompanying drawings, in which preferred embodiments of the invention are shown. This invention may, however, be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey the scope of the invention to those skilled in the art. Like numbers refer to like elements throughout.

As will be appreciated by one of skill in the art, the present invention may be embodied as a method, data processing system, or computer program product. Accordingly, the present invention may take the form of an entirely hardware embodiment, an entirely software embodiment, or an embodiment combining software and hardware aspects. Furthermore, the present invention may take the form of a computer program product on a computer-usable storage medium having computer readable program code means embodied in the medium. Any suitable computer readable medium may be utilized including, but not limited to, hard disks, CD-ROMs, optical storage devices, and magnetic storage devices.

The present invention is described below with reference to flowchart illustrations of methods,

apparatus (systems), and computer program products according to an embodiment of the invention. It will be understood that each block of the flowchart illustrations, and combinations of blocks in the flowchart illustrations, can be implemented by computer program instructions. These computer program instructions may be provided to a processor of a general purpose computer, special purpose computer, or other programmable data processing apparatus to produce a machine, such that the instructions, which execute via the processor of the computer or other programmable data processing apparatus, create means for implementing the functions specified in the flowchart block or blocks.

These computer program instructions may also be stored in a computer-readable memory that can direct a computer or other programmable data processing apparatus to function in a particular manner, such that the instructions stored in the computer-readable memory produce an article of manufacture including instruction means which implement the function specified in the flowchart block or blocks.

The computer program instructions may also be loaded onto a computer or other programmable data processing apparatus to cause a series of operational steps to be performed on the computer or other programmable apparatus to produce a computer implemented process such that the instructions which execute on the computer or other programmable apparatus provide steps for implementing the functions specified in the flowchart block or blocks.

A method of the instant invention is illustrated in **Fig. 1**. In the first step **10**, the patient is examined to determine patient information. Examples of patient information that may be gathered include one or more of gender, age, weight, CD4⁺ cell information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, and information for drug treatments for other conditions. The information may include historical information on prior therapeutic treatment regimens for the disease or medical condition. While the patient is typically examined on a first visit to determine the patient information, it will be appreciated that patient information may also be stored in the computing device, or transferred to the computing device from another computing device, storage device, or hard copy, when the information has been previously determined.

The patient information is then provided **11** to a computing device that contains a knowledge base of treatments, contains a knowledge base of expert rules for determining available treatment options for the patient in light of the patient information, and also contains a knowledge base of advisory information. A list of available treatments for the patient is then generated **12** from the patient information and the available treatments by the expert rules, and advisory information for the available treatments is generated **13**. The advisory information may include warnings to

take the patient off a contraindicated drug or select a suitable non contraindicated drug to treat the condition before initiating a corresponding treatment regimen and/or information clinically useful to implement a corresponding therapeutic treatment regimen.

For example, when the known disease is HIV-1 infection, the treatment regimen includes antiretroviral drugs, and the treatment regimen or advisory information may also include contraindicated or potentially adversely interacting non-antiretroviral drugs. Particularly, when the treatment regimen includes a protease inhibitor. A contraindicated drug may be terfenadine. When the treatment regimen includes indinavir, a contraindicated drug is cisapride.

Exemplary antiretroviral drugs are listed below in **Table 1**.

Table 1

Abbreviation	Formal Name	Generic Name
ABC	ZIAGEN®	Abacavir
ADV	PREVEON®	Adefovir
APV	AGENERASE®	Amprenavir
AZT	RETROVIR®	Zidovudine
ddI	VIDEX®	Didanosine
ddC	HIVID®	Zalcitabine
d4T	ZERIT®	Stavudine
EFV	SUSTIVA®	Efavirenz
3TC	EPIVIR®	Lamivudine
SQV	INVIRASE®/ FORTOVASE®	Saquinavir
IDV	CRIXIVAN®	Indinavir
RTV	NORVIR®	Ritonavir
DLV	RESCRIPTOR®	Delavirdine
NFV	VIRACEPT®	Nelfinavir
NVP	VIRAMUNE®	Nevirapine

Exemplary advisory information that can be displayed to a user is summarized below in **Table 2**.

Table 2

	Description
Drug Therapies (All the output data types below are associated with a therapy)	The inference engine will process every therapy from a resource file which contains all valid therapy combinations. The system will support multiple drug combinations. Those therapies which are recommended by the knowledge base will be displayed along with all the data types below.
Commentaries	Commentaries consist of warnings and advisories concerning drugs as well as various patient conditions. Each commentary will appear in specific locations of the User Interface. Commentaries will have various Flags, Triggers, and Output Locations.
Rejection Notices	Rejection Notices are the explanation why a given therapy is not recommended. Rejection notices always appear in predefined places in the User Interface.
Cost	The cost per day is calculated for each therapy by the inference engine as well as each drug cost within a therapy.
Dosage	The base dosage and any adjustments to the base dosage due to various patient conditions are calculated by the inference engine.
Pill Burden	The number of pills in the therapy.
Frequency	Number of times the patient will be taking medications for a given therapy. For a multi-drug therapy, the Frequency of the therapy is the drug in the therapy that has the highest number of Frequencies. If a three-drug regimen has 2 drugs with q12h dosages and one that is a q8h, the therapy is considered to be a q8h Frequency.
Admin	Special drug administration instructions.
Efficacy	The relative Efficacy is a whole number that represents the relative efficacy of the various therapies. One is the most effective therapy.
Adjusted Score	The "Adjusted Score" is the Efficacy adjusted up or down based on patient specific characteristics to roughly indicate the likelihood of that therapy being an effective treatment for that patient. An example would be: the system evaluates a therapy containing a drug that is known to be associated with a medical condition in that patient's medical history, therefore the therapy is ranked low. The Ranking Ordinal is an integer, beginning with 0 and

	having no upper limit. A therapy with a 1 Ranking Ordinal (RO=1) would be ranked at the top of the list whereas a therapy with a 10 Ranking Ordinal (RO=10) would be less likely to be successful given the patient's specific history and characteristics. Each therapy will have a starting RO number which will be the therapy's relative efficacy score. The relative efficacy score can then be adjusted up or down by the rules. Both base "Efficacy" number and the "Adjusted Score" number can be displayed.
--	--

Diseases (or medical conditions), the treatment of which may be facilitated or improved by the present invention, are those for which multiple different therapy options are available for selection and treatment. Such diseases and medical conditions include, but are not limited to, cardiovascular disease (including but not limited to congestive heart failure, hypertension, hyperlipidemia and angina), pulmonary disease (including but not limited to chronic obstructive pulmonary disease, asthma, pneumonia, cystic fibrosis, and tuberculosis), neurologic disease (including but not limited to Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, amyotrophic lateral sclerosis or ALS, psychoses such as schizophrenia and organic brain syndrome, neuroses, including anxiety, depression and bipolar disorder), hepatitis infections (including hepatitis B and hepatitis C infection), urinary tract infections, venereal disease, cancer (including but not limited to breast, lung, prostate, and colon cancer), etc. It should be appreciated that prevention of development or onset of the above-mentioned diseases and medical conditions may be facilitated or improved by the present invention.

5 The present invention is useful for known
diseases such as HIV-1 infection (acquired immune
deficiency syndrome or "AIDS"), or where the known
disease is any medical condition for which a
combination therapeutic treatment regimen can be used.
The invention is particularly useful when the list of
available treatments includes a plurality (e.g., 2, 10
or 15 or more) of treatment, combination therapeutic
treatment regimens (e.g., therapeutic treatment
10 regimens incorporating two or more active therapeutic
agents), where the potential for drug interactions is
increased and/or the complexity involved in selecting
the best available treatment is multifactorial.

Advantageously, the list of available
15 treatments and advisory information may be regenerated
in a number of ways. The patient information may be
simply modified 18. In addition, if a particular
therapy in which the user might be interested is not
presented, a user-defined therapy may be entered 14 and
20 advisory information generated 15 based on the user-
defined therapy. Still further, if a therapeutic
treatment regimen that is in the knowledge base is
rejected by the system (not recommended upon display),
the non-recommended therapeutic treatment regimen may
25 be entered 16 and advisory information generated 17 for
the non-recommended therapeutic treatment regimen. This
may indicate to the user that they should discontinue
use of a non-critical drug for another condition or
select a suitable substitute that does not create a
30 conflict/non-recommended situation so that they can
then proceed with the therapy of choice. Alternatively,

the advisory information can be generated automatically for non-recommended therapeutic treatment regimens. These various steps can be repeated in any sequence in an interactive manner to provide the user with assurance that all treatment options have been given adequate and appropriate consideration.

The terms "therapy" and "therapeutic treatment regimen" are interchangeable herein and, as used herein, mean any pharmaceutical or drug therapy, regardless of the route of delivery (e.g., oral, intravenous, intramuscular, subcutaneous, intraarterial, intraperitoneal, intrathecal, etc.), for any disease (including both chronic and acute medical conditions, disorders, and the like). In addition, it is understood that the present invention is not limited to facilitating or improving the treatment of diseases. The present invention may be utilized to facilitate or improve the treatment of patients having various medical conditions, without limitation.

System Description

The present invention may be embodied as an expert system that provides decision support to physicians (or other health care providers) treating patients with a known disease, such as HIV infection. A system according to the present invention calculates combination antiretroviral therapy options and attaches all relevant information to those options.

As known to those of skill in the art, an expert system, also known as artificial intelligence (AI), is a computer program that can simulate the

judgment and behavior of a human or an organization that has expert knowledge and experience in a particular field. An expert system typically contains a knowledge base containing accumulated experience and a set of rules for applying the knowledge base to each particular situation that is described to the program. Expert systems are well known to those of skill in the art and need not be described further herein.

The antiretroviral therapy options (combinations of antiretroviral drugs), are derived using a knowledge base consisting of a number of expert system rules and functions which in turn take into account a given patient's treatment history, current condition and laboratory values. A system according to the present invention supports the entry, storage, and analysis of patient data in a large central database. A system according to the present invention has a flexible data driven architecture and custom reporting capabilities designed to support patient therapy management and clinical drug trial activities such as screening, patient tracking and support. It is anticipated that a system according to the present invention may be used by health care providers (including physicians), clinical research scientists, and possibly healthcare organizations seeking to find the most cost-effective treatment options for patients while providing the highest standard of care.

A system 20 for carrying out the present invention is schematically illustrated in **Fig. 2**. The system 20 comprises a knowledge base of treatment regimens 21, which may be ranked for efficacy (e.g., by

a fuzzy inference engine).

High-speed inference engines are preferred so that the results of data entered are continually updated as new data is entered. As with the knowledge bases and patient information in blocks 21-25, the inference engine 26 may be a separate block from the knowledge bases and patient information blocks 21-25, or may be combined together in a common program or routine.

Note that the advisory information that is generated for any available therapy may differ from instance to instance based on differences in the patient information provided.

System Architecture

The present invention can be implemented as a system running on a stand alone computing device. Preferably, the present invention is implemented as a system in a client-server environment. As is known to those of skill in the art, a client application is the requesting program in a client-server relationship. A server application is a program that awaits and fulfills requests from client programs in the same or other computers. Client-server environments may include public networks, such as the Internet, and private networks often referred to as "intranets", local area networks (LANs) and wide area networks (WANs), virtual private networks (VPNs), frame relay or direct telephone connections. It is understood that a client application or server application, including computers hosting client and server applications, or other

apparatus configured to execute program code embodied within computer usable media, operates as means for performing the various functions and carries out the methods of the various operations of the present invention.

Referring now to **Fig. 3**, a client-server environment 30 according to a preferred embodiment of the present invention is illustrated. The illustrated client-server environment 30 includes a central server 32 that is accessible by at least one local server 34 via a computer network 36, such as the Internet. A variety of computer network transport protocols including, but not limited to TCP/IP, can be utilized for communicating between the central server 32 and the local servers 34.

Central Server

The central server 32 includes a central database 38, such as the Microsoft® SQL Server application program, version 6.5 (available from Microsoft, Inc., Redmond, WA), executing thereon. The central server 32 ensures that the local servers 34 are running the most recent version of a knowledge base. The central server 32 also stores all patient data and performs various administrative functions including adding and deleting local servers and users to the system (20, **Fig. 2**). The central server 32 also provides authorization before a local server 34 can be utilized by a user. Patient data is preferably stored on the central server 32, thereby providing a central repository of patient data. However, it is understood

that patient data can be stored on a local server 34 or on local storage media.

Local Server

5 Each local server 34 typically serves multiple users in a geographical location. Each local server 34 includes a server application, an inference engine, one or more knowledge bases, and a local database 39. Each local server 34 performs artificial
10 intelligence processing for carrying out operations of the present invention. When a user logs on to a local server 34 via a client 35, the user is preferably authenticated via an identification and password, as would be understood by those skilled in the art. Once
15 authenticated, a user is permitted access to the system (20, Fig. 2) and certain administrative privileges are assigned to the user.

Each local server 34 also communicates with the central server 32 to verify that the most up-to-
20 date version of the knowledge base(s) and application are running on the requesting local server 34. If not, the requesting local server 34 downloads from the central server 32 the latest validated knowledge base(s) and/or application before a user session is
25 established. Once a user has logged onto the system (20, Fig. 2) and has established a user session, all data and artificial intelligence processing is preferably performed on a local server 34. An advantage of the illustrated client-server configuration is that
30 most of the computationally intensive work occurs on a local server 34, thereby allowing "thin" clients 35

(i.e., computing devices having minimal hardware) and optimizing system speed.

In a preferred embodiment, each local server database 39 is implemented via a Microsoft® SQL Server application program, Version 6.5. The primary purpose of each local database 39 is to store various patient identifiers and to ensure secure and authorized access to the system (20, Fig. 2) by a user. It is to be understood, however, that both central and local databases 38, 39 may be hosted on the central server 32.

Local Client

Each local client 35 also includes a client application program that consists of a graphical user interface (GUI) and a middle layer program that communicates with a local server 34. Program code for the client application program may execute entirely on a local client 35, or it may execute partly on a local client 35 and partly on a local server 34. As will be described below, a user interacts with the system (20, Fig. 2) by entering (or accessing) patient data within a GUI displayed within the client 35. The client 35 then communicates with a local server 34 for analysis of the displayed patient information.

Computer program code for carrying out operations of the present invention is preferably written in an object oriented programming language such as JAVA®, Smalltalk, or C++. However, the computer program code for carrying out operations of the present invention may also be written in conventional

procedural programming languages, such as the "C"
programming language, in an interpreted scripting
language, such as Perl, or in a functional (or fourth
generation) programming language such as Lisp, SML, or
Forth.

The middle layer program of the client
application includes an inference engine within a local
server 34 that provides continuous on-line direction to
users, and can instantly warn a user when a patient is
assigned drugs or a medical condition that is
contraindicated with, or antagonistic of, the patient's
current antiretroviral therapy. Every time patient data
is entered into the system (20, Fig. 2) or updated, or
even as time passes, the inference engine evaluates the
current status of the patient data, sorting,
categorizing, ranking and customizing every possible
antiretroviral therapy for a patient according to the
specific needs of the patient.

Inference Engine

Inference engines are well known by those of
skill in the art and need not be described further
herein. Each knowledge base used by an inference engine
according to the present invention is a collection of
rules and methods authored by a clinical advisory panel
of HIV-treating physicians and scientists. A knowledge
base may have subjective rules, objective rules, and
system-generated rules. Objective rules are based on
industry established facts regarding the treatment of
HIV using antiretroviral therapy and are drawn from the
package insert information of antiretroviral drug

manufacturers and from peer reviewed and published journal articles. An example of an objective rule would be an antiretroviral to antiretroviral contraindication such as:

5

Rule #1: If the eval therapy contains Zidovudine (AZT) and Stavudine (d4T), then reject the therapy.

10 In Rule #1, the term "eval therapy" refers to the therapy currently being analyzed by the system (20, **Fig. 2**). Rule #1 then states that if this therapy contains both AZT and d4T, then this therapy should not be displayed in a list of potential therapy options for the patient.

15

For objective rules, the present invention can be configured so as to prevent a user from receiving recommendations on new therapy options when certain crucial data on the patient has not been entered. However, it is understood that the present invention does not prevent a health care provider, such as a physician, from recording his/her therapy decisions, even if the system (20, **Fig. 2**) has shown reasons why that therapy may be harmful to the patient.

20

25 The present invention allows a health care provider to be the final authority regarding patient therapy.

25

Subjective rules are based on expert opinions, observations and experience. Subjective rules are typically developed from "best practices" information based on consensus opinion of experts in the field. Such expert opinion may be based on knowledge of the literature published or presented in

30

the field or their own experience from clinical practice, research or clinical trials of approved and unapproved medications. A number of experts are used so that personal bias is reduced.

5 System generated rules are those derived from the outcomes of patients tracked in the system who received known and defined therapies and either improved, stabilized or worsened during a defined period. Because of the large number of potential
10 combinations usable in HIV infection, this system generated database and rules derived from them are likely to encompass data beyond that achievable from objective or subjective rules databases.

 The rules which comprise the various
15 knowledge bases (21-24, Fig. 2) of the present invention each have two main parts: a premise and a conclusion - also referred to as the left side and the right side, respectively. When a premise of a rule is found to be true, the action specified in the
20 conclusion is taken. This is known to those of skill in the art as "firing" the rule. For example, consider the following rule:

<u>Rule ID</u>	<u>Premise</u>	<u>Conclusion</u>
25 FiltDComA1	-- If the eval therapy contains ddC	- Commentary 18

The premise of the above rule is for the inference engine to determine whether or not a therapy being evaluated (i.e., "eval therapy") contains the
30 antiretroviral drug "ddC". If a therapy does contain the antiretroviral drug ddC, the action called for by the conclusion of the rule is to attach "Commentary 18"

to the therapy. Commentary 18 may be a piece of text that provides a user with the necessary information about therapies containing ddC.

5 Exemplary rules which may comprise one or more knowledge bases according to the present invention are listed below in **Table 3**.

Table 3

Therapy initiation/change: Rules that provide information on therapy change or initiation
Boundary condition rules: Limits for values, intervals for values to be updated
Comment Data Aging rules: These rules warn the user that the data in certain fields is getting old and that the most current values in the system will be used.
Rules that filter therapies due to drug interactions in ARV drug combinations
Rules that filter therapies due to medical conditions
Rules that filter therapies due to genotypic mutations in patient's plasma HIV
Rules that filter therapies due to phenotypic sensitivity/resistance
Antiretroviral therapy ranking rules
General dosage rules
Solid dosage rule
Dosage modifications due to ARV-ARV drug combination
Dosage modification due to ARV-NonARV interaction
Dosage modification due to medical condition
Comment determined
General commentary rules
Commentaries added due to medical conditions
Commentaries added due to drug interactions

Commentaries added due to drug combination

Delivery size rules

Using the various knowledge bases and patient information of the present invention (21-25, Fig. 2), the inference engine (26, Fig. 2) can evaluate potential therapy options for a patient based on a patient's medical history (including therapy history) and current laboratory values. Accordingly multiple antiretroviral drug combinations can be quickly and accurately analyzed for a particular patient. Furthermore, the inference engine can quickly provide guidance in the areas listed below in Table 4.

Table 4

Data Integrity	Is the patient lab and assessment data getting too old to be considered reliable? Are there conflicts between lab data such as phenotype data which indicates resistance to one or more antiretroviral drugs in the patient's current therapy and current viral load data which indicates significant viral suppression?
Therapy Performance	Should antiretroviral therapy be initiated for the patient? Is the patient's current therapy achieving good initial and long-term viral suppression or should the therapy be changed? Are there potential non-compliance issues as demonstrated by a lack of viral suppression with a regimen when current genotype or phenotype data does provide explanation for the failure by demonstrating resistance to any drugs in the patient current therapy?
Dosage	What are the base and adjusted dosages of antiretroviral drugs in a given therapy? Are there any special specific dosage administration instructions? What are options if patient can only take liquid dosage forms?
Contra-indications	Which antiretroviral drugs can be used with each other and what dosage adjustments are

	required? Are there any contraindications or interactions between antiretroviral drugs in patient's current therapy or potential therapies and the non-antiretroviral drugs patient is taking and if so what are they and what, if any, dosage adjustments are required?
Medical Conditions	Are there any medical conditions to be aware of in deciding an appropriate therapy for patient? What, if any, effect do current or historical medical conditions have on each therapy option?
Drug Cost and Delivery Data	How much does each therapy option cost? What is the dosing frequency of the drugs in the therapy? What is the pill count and optimum delivery size for the least number of pills?
Therapy Options	What are all the drug combination therapy options for patient? How can physician instantly assess which of the hundreds of potential combinations will be the most effective for patient? What information from the package inserts from each drug apply specifically to patient? What is the relative antiviral efficacy of each therapy? Are there special considerations that might make one therapy more or effective for patient?
Resistance	What drugs are patient's virus current genotypic or phenotypic profile known to be associated with resistance to? Which antiretroviral drugs are more effective against resistant strains when used together? Which drugs (if any) used in historical therapies are most likely to be effective if recycled into a new therapy? Can any of the drugs in patient's current therapy be recycled into the next therapy?

User Interface

Referring now to **Figs. 4-9**, exemplary user interfaces according to the present invention will be illustrated. In **Fig. 4**, a medical history user interface 50 for entering data about a patient's medical history according to the present invention is

illustrated. The medical history user interface 50 can be displayed by activating the "Medical History" tab 50a. The illustrated medical history user interface 50 allows a user to create, save, update and print patient records. When a user adds a new patient, the medical history user interface 50 appears with empty data entry fields. Data entry fields for receiving information via a GUI are well known to those of skill in the art and need not be described further herein. When a user opens a patient record for editing, the medical history user interface 50 appears with patient data in the various fields. Preferably color is used to highlight critical or required information in a patient record.

Important elements in the illustrated medical history user interface 50 include a "print" button 51 for printing a patient record and therapeutic treatment regimen details; a "save" button 52 for saving a patient record; and a "speed entry" check box 53 for allowing a user to move quickly between entry fields. In addition, there are multiple group headings 54 that divide a patient's medical history into related categories. Each group contains entry fields in which a user can add patient information. An "add" button 55 allows a user to add new information to a patient record for a selected group. A "delete" button 56 allows a user to delete patient information for a selected group (although the original information is still recorded in the database). A "history" button 57 allows a user to review a patient's historical data for each selected group.

After completing a patient's medical history,

an inference engine analyzes the data and suggests whether a therapeutic treatment regimen is indicated; if an existing therapeutic treatment regimen should be continued or changed; and the best drug therapies for the selected patient. Often, more than one drug therapy is presented to the user. These drug therapies are preferably ranked according to expected efficacy, frequency in dosage, pill count, and cost. All of these factors can help the user make a decision about what therapy to use for the selected patient. When a user clicks on a drug therapy in the presented list, information is provided about the dosage regimens. Also, various warnings, such as drug interaction warnings, and notes about each drug, are presented. An appropriate drug therapy can then be selected.

In **Fig. 5**, an exemplary user interface chart **60** for monitoring a patient's condition during a particular drug therapy over a period of time is illustrated. The user interface chart **60** can be displayed by activating the "Chart" tab **60a**. The illustrated user interface chart **60** tracks the CD4 level against viral load. Along the left-hand side of the Y-axis **61** the CD4 count is plotted. Along the right-hand side of the Y-axis **61** the viral load count is plotted. The lines **62** represent the CD4 test and the viral load test as would be understood by those having skill in the art. Drug therapy for a time period is indicated within the area of the chart user interface **60** indicated as **63**. Time is plotted along the X-axis **64**, as illustrated.

In **Fig. 6**, a therapy evaluation user

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interface **70** that facilitates evaluation of various therapy options with respect to relative efficacy, dosage, frequency, cost, medical complications and drug interactions is illustrated. The therapy evaluation user interface **70** can be displayed by activating the "Therapy Evaluation" tab **70a**. Important elements in the illustrated therapy evaluation user interface **70** include an "Evaluate Current Therapy" button **71** for initiating an evaluation of a current therapy and a "Current Therapy" field **72** that lists a patient's current therapy. Detailed information about a patient's therapy is displayed in the therapy details box **73**. A therapy displayed within box **73** is identified in box **74**.

Multiple check boxes **75** are provided that allow a user to control how information is displayed within the therapy evaluation user interface **70**. Within the therapy list box **76**, a list of available therapies for a patient can be displayed. In the illustrated embodiment the drugs are listed in standard abbreviated form. Other information displayed with each drug may include that listed below in **Table 5**.

Table 5

Efficacy Rating	Lists the therapy according to expected effectiveness only, regardless of patient specific considerations (1 is most effective).
Adjusted Score	This number uses the Efficacy Rating as a base and then the system adjusts it up or down based on patient specific conditions (1 is most effective).
Safety Considerations	A brief two or three word summary of the alerts associated with the therapy.
Frequency	Lists the dosage frequency (q12h, q24h, etc.).
Pills	Lists the total number of pills required per day for

	the complete regimen.
Cost	Lists the total cost of the regimen per day.
Medical Alert	Displays a Y if there is one or more Yellow Medical Alerts and an R if there is one or more Red Medical Alerts associated with the therapy.
Drug Interaction	Displays a Y if there is one or more Yellow Drug Interaction Alerts and an R if there is one or more Red Drug Interaction Alerts associated with the therapy.

A list of available antiretroviral drugs is displayed within box 77. A user desiring to evaluate a particular combination of drugs can click the appropriate check boxes 77a to review information in the therapy details box 73. A "Use as Current Therapy" button 78 allows a user to apply a particular therapy to a patient. Various hyperlinks 79 within the therapy details box 73 allow a user to display specific information about a therapy evaluation. For example, a user can be allowed to view a rule which is associated with the displayed text.

Resistance evaluation alerts 80 can be provided adjacent each available antiretroviral drug displayed within box 77. For example, a blue "G" icon can be used to indicate that a patient's last genotype test contains mutations which are known to be associated with full or partial resistance to the antiretroviral drug. A red "P" icon can be used to indicate that a patient's last phenotype test demonstrates resistance to the antiretroviral drug.

Within the therapy list box 76, various symbols (described in Fig. 7) can be utilized to provide information about a drug therapy option. These symbols provide an instant graphical warning level for

each therapy option. Some symbols, such as a red exclamation point, indicate that there is critical, possibly life threatening information in the therapy details box 73 for that therapy which must be read in order for that therapy to be properly utilized.

When a drug therapy from the therapy list box 76 is selected by a user for evaluation, the therapy details box 73 of **Fig. 6** can be displayed in "full screen" mode as illustrated in **Fig. 8**. Important elements in the illustrated therapy details box 73 include an identification box 73a for identifying the therapy being evaluated; a "Use as Current Therapy" button 78 that allows a user to apply a particular therapy to a patient; and a "Show Therapies" button 73b that returns the therapy details box 73 back to half-screen size as illustrated in **Fig. 6**. In addition, various hyperlinks may be embedded within text displayed within the therapy details box 73 that can be activated by a user to display various types of information. Eye catching alert banner(s) 73c and text 73d can be displayed at the top of the therapy details box 73 as illustrated. Dosages 73e of each drug, along with special administration instructions, can be displayed within the therapy details box 73 as illustrated. Dosage adjustment information 73f and various warnings and advisories 73g can also be displayed within the therapy details box 73 as illustrated.

According to a preferred embodiment of the present invention, therapeutic treatment regimens are not displayed to a user if an invalid drug is selected

for treatment of a patient.

Physicians Desk Reference®

According to a preferred embodiment of the present invention, the Physicians Desk Reference® (PDR®) 28, which is a known drug reference source, is fully integrated with the system 20 of Fig. 2. Users can access the PDR® drug abstracts for antiretroviral drugs listed in the therapy list box 76 of the therapy evaluation user interface 70 of Fig. 6. In addition, users can access the PDR® on-line Web database to obtain additional information about a specific drug or to research a substitute for a contraindicated drug. When a user selects a drug within the therapy list box 76 of the therapy evaluation user interface 70, a web browser preferably is launched and the PDR® on-line Web database is accessed. Information can also be extracted from the PDR® on-line Web database to provide drug selection lists for non-antiretroviral drugs that a patient may be taking and to define relationships between brand name and generic drugs.

As illustrated in Fig. 9, a PDR® pop-up menu 90 may be provided that can be activated from within the therapy list box 76 of the therapy evaluation user interface 70 of Fig. 6. From the PDR® pop-up menu 90 a user can access various information from the PDR® including, but not limited to, drug abstracts, and generic components contained within a brand name drug.

The following non-limiting examples illustrate various aspects of the present invention. These examples are provided for illustrative purposes

only, and are not intended to be limiting of the invention.

EXAMPLE 1

5 Example 1 will be explained with reference to
Figs. 10A-10D. Referring to **Fig. 10A**, a medical history
user interface **50** containing evaluated data for patient
"demo1" is illustrated. The group heading "Hemoglobin"
10 **54a** has changed colors to indicate to a user that the
patient has an abnormally low hemoglobin value from a
previous (historical) blood sampling. When the therapy
evaluation tab **70a** is activated to display the therapy
evaluation user interface **70** (**Fig. 10B**) the associated
medical condition warning of a history of anemia and
15 the caution notification if using drugs known to be
associated with hematopoietic toxicity is triggered as
illustrated in the therapy details box **73** of **Fig. 10B**.

 In addition, the group heading "Renal
Function" **54b** in **Fig. 10A** has changed colors to warn a
20 user of potential renal dysfunction and is also
indicated by the low estimated creatinine clearance
rate in field **F1** (which the system calculates using a
mathematical formula taking patient age, sex, weight,
and serum creatinine values - all of which are fields
25 of the "Medical History" user interface **50**). This
information is pointed out to the user and is used if
dosage adjustments are required for drugs that are
known to be affected (cleared) by renal function.

 Current and the next most recent CD4⁺ cell
30 count and viral load are displayed (**F2**, medical history
user interface **50**). This information is also used to

determine when to start or change therapy and to evaluate the initial antiviral efficacy of a newly administered antiviral regimen.

Current and historical values for all fields in the medical history user interface 50 (**Fig. 10A**) can be viewed by pressing the "H" button beside fields that have this button.

In **Fig. 10C**, the "Chart" user interface 60 has been activated. HIV RNA (viral load) is plotted on a log scale, the CD4 count is plotted on a linear scale, and the drug treatments are shown as Gantt bars on the horizontal date scale at the bottom of the chart user interface 60.

In **Fig. 10D**, the "Change Therapy Recommendation" message box **MB1** pops up when the "Therapy Evaluation" tab 70a is selected. This box represents the processing of the data from the "Medical History" tab and the knowledge base output, including objective rules derived from published treatment guidelines, indicating that initiation of therapy, or a change of therapy in this case, may be called for if the other variable(s) indicated in the message have been addressed.

The list of available therapies and associated ranking order may be shown within the therapy details box 73 of **Fig. 10B**. This represents the output of the knowledge base for therapy selection. Included with the list of therapies can be any of the following: safety advisories (dosage adjustment, drug interaction, etc.) with a yellow triangle or red exclamation warning symbols; number of pills; daily

cost of all three drugs; dosing regimen (q 8h, q 12 h, etc.); and dosages for all drugs in a regimen (including dosage adjustments if necessary) and pertinent information specific to the patient is listed in the dialog box.

EXAMPLE 2

Example 2 will be explained with reference to **Figs. 11A-11E**, and relates to patient file "ARV naive1" which is an example of an HIV-infected patient who has not been treated with anti-HIV drugs previously. In **Fig. 11A**, a medical history user interface 50 containing evaluated data for patient "ARV naive1" is illustrated. In **Fig. 11B**, when the "Therapy Evaluation" tab 70a is activated to display the therapy evaluation user interface 70, a "Boundary and Prequalification Messages" message box MB2 pops up indicating that according to the current, published, HIV treatment guidelines, the patient should be initiated on antiviral therapy and that the current guidelines recommend combinational therapy.

In **Fig. 11C**, the therapy evaluation user interface 70 has been activated and demonstrates features/functions associated with therapy evaluation including a general warning W1 and advisories A1, A2, and A3 for the patient related to treatment of the disease (e.g., whether therapy should be initiated or changed) or related to a specific therapy selected from the list box which is being evaluated by the user.

Fig. 11D illustrates various information that is displayable by clicking on an individual therapy in

the therapy list box 76 of **Fig. 11C**. Information displayed includes dosages of all drugs with general and patient-specific warnings and advisories.

The features available by right clicking on any therapy listed in the therapy list box 76 of **Fig. 11C** are illustrated in **Fig. 11E** and include: linking to an electronic PDR® to show drug package insert information or perform drug search information; showing or hiding columns of information displayed within the therapy list box; linking to a publication or abstract associated with a therapy that has a "book" icon associated therewith; and various printing functions.

EXAMPLE 3

Example 3 will be explained with reference to **Figs. 12A-12C**, and relates to patient file "Features1" which illustrates some important functions/features that a system according to the present invention can provide for highly drug experienced patients who may have developed resistance associated with the use of several antiviral drugs. Features, including functions attributed to the new resistance and historical therapy rules are illustrated and includes:

- 1) Potential drug resistance advisories (**A1, Fig. 12A**) when the chart tab 60a is activated, or (**A2, Fig. 12B**) when the therapy evaluation tab 70a is activated;
- 2) The heads up "P" and "G" indicators (**I1 and I2, Fig. 12B**) to remind of phenotypic or genotypic resistance associated with certain anti-HIV compounds as

demonstrated for this patient (including indication of expected/anticipated genotypic resistance, as a result of cross-resistance, to a drug that a patient may not be taking currently or has not previously taken);

5

3) The drug interaction warning system (indicated by warning **W3**, **Fig. 12C**). Warning **W3** is for the interaction between Nevirapine and rifabutin (which was selected from the list of non-antiretroviral drugs available as part of the medical history user interface **50**). The drug interaction warning message may be viewed from the medical history user interface **50** by "right-clicking" the non-ARV title bar **54C**, which has turned yellow indicating the presence of an ARV-nonARV drug interaction. This information is also prominently displayed for the user on the therapy evaluation user interface **70** as a text message (**W3**, **Fig. 12B**) as well as in the "Safety Considerations" section of the drug list box (**76**, **Fig. 12B**); and

10

15

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4) The chart user interface **60** (**Fig. 12A**) illustrates the viral load, CD4, drug therapies, and associated drug resistance in graphic form for the user to evaluate.

25

The foregoing is illustrative of the present invention and is not to be construed as limiting thereof. Although a few exemplary embodiments of this invention have been described, those skilled in the art will readily appreciate that many modifications are possible in the exemplary embodiments without materially departing from the novel teachings and

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advantages of this invention. Accordingly, all such
modifications are intended to be included within the
scope of this invention as defined in the claims.
Therefore, it is to be understood that the foregoing is
5 illustrative of the present invention and is not to be
construed as limited to the specific embodiments
disclosed, and that modifications to the disclosed
embodiments, as well as other embodiments, are intended
to be included within the scope of the appended claims.
10 The invention is defined by the following claims, with
equivalents of the claims to be included therein.

THAT WHICH IS CLAIMED IS:

1. A method for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said method comprising:

5 (a) providing patient information to a computing device comprising:

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10 a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for evaluating and selecting a therapeutic treatment regimen for said disease or medical condition;

15 a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of said different therapeutic treatment regimens; and

20 (b) generating in said computing device a listing of available therapeutic treatment regimens for said patient; and

25 (c) generating in said computing device advisory information for one or more therapeutic treatment regimens in said listing based on said patient information and said expert rules.

2. A method according to claim 1, further

comprising the steps of:

(d) entering a user-defined therapeutic treatment regimen for said disease or medical condition that is not included in said first knowledge base;

(e) generating in said computing device advisory information for said user-defined combination therapeutic treatment regimen.

3. A method according to claim 1, further comprising the steps of:

(f) entering a non-recommended therapeutic treatment regimen for said disease or medical condition that is included in said first knowledge base but not recommended from said listing; and

(g) generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

4. A method according to claim 1, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, and information for drug treatments for other conditions.

5. A method according to claim 1, said patient information including prior therapeutic treatment regimen information.

6. A method according to claim 1, wherein
said listing of available therapeutic treatment
regimens for said patient comprises a ranked listing of
available therapeutic treatment regimens for said
5 patient.

7. A method according to claim 1, wherein
said patient information includes prior patient
information stored in said computing device.

8. A method according to claim 1, said
advisory information including:

warnings to take the patient off a
contraindicated drug before initiating a corresponding
therapeutic treatment regimen; and
5

information clinically useful to implement a
corresponding therapeutic treatment regimen.

9. A method according to claim 1, wherein
said computing device comprises a fourth knowledge base
comprising patient therapeutic treatment regimen
history, said advisory information including previous
5 therapeutic treatment regimen information extracted
from said fourth knowledge base.

10. A method according to claim 8, wherein
said known disease or medical condition is HIV-1
infection, said therapeutic treatment regimen includes
antiretroviral drugs, and said therapeutic treatment
5 regimen includes contraindicated or potentially
adversely interacting non-antiretroviral drugs.

11. A method according to claim 8, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

12. A method according to claim 8, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

13. A method according to claim 1, wherein said known disease or medical condition is one where multiple prophylactic or therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease.

14. A method according to claim 1, wherein said known disease or medical condition is a cardiovascular disease.

15. A method according to claim 1, wherein said known disease or medical condition is a pulmonary disease.

16. A method according to claim 1, wherein said known disease or medical condition is a neurologic disease.

17. A method according to claim 1, wherein said known disease or medical condition is cancer.

18. A method according to claim 1, wherein said known disease or medical condition is a urinary

tract infection.

19. A method according to claim 1, wherein said known disease or medical condition is hepatitis.

20. A method according to claim 1, wherein said known disease or medical condition is HIV-1 infection.

21. A method according to claim 1, wherein said knowledge base comprises a plurality of different combination therapeutic treatment regimens.

22. A method according to claim 1, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

23. A method according to claim 1, further comprising the step of:

(d) accessing, via said computing device, information for one or more therapeutic treatment regimens from a drug reference source.

24. A system for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said system comprising:

- 5 (a) a computing device comprising:
a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

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10 a second knowledge base comprising a
 plurality of expert rules for selecting a
 therapeutic treatment regimen for said
 disease or medical condition;
 a third knowledge base comprising
15 advisory information useful for the treatment
 of a patient with different constituents of
 said different therapeutic treatment
 regimens; and
 (b) means for providing patient information
20 to said computing device;
 (c) means for generating in said computing
 device a listing of therapeutic treatment regimens for
 said patient; and
 (d) means for generating in said computing
25 device advisory information for one or more therapeutic
 treatment regimens in said listing based on said
 patient information and said expert rules.

25. A system according to claim 24, further
comprising:

 (e) means for entering a user-defined
therapeutic treatment regimen for said disease or
5 medical condition that is not generated or displayed
 via said first knowledge base;

 (f) means for generating in said computing
device advisory information for said user-defined
combination therapeutic treatment regimen.

26. A system according to claim 24, further
comprising:

 (f) means for entering a non-recommended

therapeutic treatment regimen for said disease or
5 medical condition that is included in said first
knowledge base but not recommended from said listing;
and

(g) means for generating in said computing
device advisory information for said non-recommended
10 therapeutic treatment regimen, said advisory
information including at least one reason for non-
recommendation of said therapeutic treatment regimen.

27. A system according to claim 24, said
patient information comprising gender, age, weight, CD4
information, viral load information, HIV genotype and
phenotype information, hemoglobin information,
5 neuropathy information, neutrophil information,
pancreatitis, hepatic function, renal function, drug
allergy and intolerance information, and information
for drug treatments for other conditions.

28. A system according to claim 24, said
patient information including prior therapeutic
treatment regimen information.

29. A system according to claim 24, wherein
said listing of available therapeutic treatment
regimens for said patient comprises a ranked listing of
available therapeutic treatment regimens for said
5 patient.

30. A system according to claim 24, wherein
said patient information includes prior patient
information stored in said computing device.

31. A system according to claim 24, said advisory information including:

warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

32. A system according to claim 24, wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

33. A system according to claim 31, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

34. A system according to claim 31, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

35. A system according to claim 31, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

36. A system according to claim 24, wherein

5 said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used singly or in combination in the treatment of said disease or medical condition.

37. A system according to claim 24, wherein said known disease or medical condition is a cardiovascular disease.

38. A system according to claim 24, wherein said known disease or medical condition is a pulmonary disease.

39. A system according to claim 24, wherein said known disease or medical condition is a neurologic disease.

40. A system according to claim 24, wherein said known disease or medical condition is cancer.

41. A system according to claim 24, wherein said known disease or medical condition is a urinary tract infection.

42. A system according to claim 24, wherein said known disease or medical condition is hepatitis.

43. A system according to claim 24, wherein said known disease or medical condition is HIV-1 infection.

44. A system according to claim 24, wherein

said knowledge base comprises a plurality of different combination therapeutic treatment regimens.

45. A system according to claim 24, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

46. A system according to claim 24, further comprising:

(e) means for accessing, via said computing device, information for one or more therapeutic treatment regimens from a standard drug reference source.

47. A computer program product for guiding the selection of a therapeutic treatment regimen for a patient with a known disease or medical condition, said computer program product comprising a computer usable storage medium having computer readable program code means embodied in the medium, the computer readable program code means comprising:

(a) computer readable program code means for generating a computing device comprising:

a first knowledge base comprising a plurality of different therapeutic treatment regimens for said disease or medical condition;

a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for said disease or medical condition;

a third knowledge base comprising

20 advisory information useful for the treatment
of a patient with different constituents of
said different therapeutic treatment
regimens; and

(b) computer readable program code means for
providing patient information to said computing device;

25 (c) computer readable program code means for
generating in said computing device a listing of
available therapeutic treatment regimens for said
patient; and

30 (d) computer readable program code means for
generating in said computing device advisory
information for one or more therapeutic treatment
regimens in said listing based on said patient
information and said expert rules.

48. A computer program product according to
claim 47, further comprising:

5 (e) computer readable program code means for
entering a user-defined therapeutic treatment regimen
for said disease or medical condition that is not
generated or displayed via said first knowledge base;

(f) computer readable program code means for
generating in said computing device advisory
information for said user-defined combination
10 therapeutic treatment regimen.

49. A computer program product according to
claim 48, further comprising:

5 (g) computer readable program code means for
entering a non-recommended therapeutic treatment
regimen for said disease or medical condition that is

included in said first knowledge base but not recommended from said listing; and

10 (h) computer readable program code means for generating in said computing device advisory information for said non-recommended therapeutic treatment regimen, said advisory information including at least one reason for non-recommendation of said therapeutic treatment regimen.

5 50. A computer program product according to claim 47, said patient information comprising gender, age, weight, CD4 information, viral load information, HIV genotype and phenotype information, hemoglobin information, neuropathy information, neutrophil information, pancreatitis, hepatic function, renal function, drug allergy and intolerance information, and information for drug treatments for other conditions.

51. A computer program product according to claim 47, said patient information including prior therapeutic treatment regimen information.

52. A computer program product according to claim 47, wherein said patient information includes prior patient information stored in said computing device.

53. A computer program product according to claim 47, said advisory information including:

5 warnings to take the patient off a contraindicated drug before initiating a corresponding therapeutic treatment regimen; and

information clinically useful to implement a corresponding therapeutic treatment regimen.

54. A computer program product according to claim 47 wherein said computing device comprises a fourth knowledge base comprising patient therapeutic treatment regimen history, said advisory information including previous therapeutic treatment regimen information extracted from said fourth knowledge base.

55. A computer program product according to claim 53, wherein said known disease or medical condition is HIV-1 infection, said therapeutic treatment regimen includes antiretroviral drugs, and said therapeutic treatment regimen includes contraindicated or potentially adversely interacting non-antiretroviral drugs.

56. A computer program product according to claim 53, wherein said therapeutic treatment regimen includes a protease inhibitor, and said contraindicated drug is terfenadine.

57. A computer program product according to claim 53, wherein said therapeutic treatment regimen includes indinavir and said contraindicated drug is cisapride.

58. A computer program product according to claim 47, wherein said known disease or medical condition is one where multiple prophylactic therapeutic treatment regimens are available to be used

5 singly or in combination in the treatment of said
disease or medical condition.

59. A computer program product according to
claim 47, wherein said known disease or medical
condition is a cardiovascular disease.

60. A computer program product according to
claim 47, wherein said known disease or medical
condition is a pulmonary disease.

61. A computer program product according to
claim 47, wherein said known disease or medical
condition is a neurologic disease.

62. A computer program product according to
claim 47, wherein said known disease or medical
condition is cancer.

63. A computer program product according to
claim 47, wherein said known disease or medical
condition is a urinary tract infection.

64. A computer program product according to
claim 47, wherein said known disease or medical
condition is hepatitis.

65. A computer program product according to
claim 47, wherein said known disease or medical
condition is HIV-1 infection.

66. A computer program product according to

claim 47, wherein said knowledge base comprises a plurality of different combination therapeutic treatment regimens.

67. A computer program product according to claim 47, wherein drug dosage information is recommended and adjusted if necessary depending upon said patient information.

68. A computer program product according to claim 47, further comprising:

(e) computer readable program code means for accessing, via said computing device, information for one or more therapeutic treatment regimens from a standard drug reference source.

69. A computer program product according to claim 47, wherein said listing of available therapeutic treatment regimens for said patient is a ranked listing of available therapeutic treatment regimens for said patient.

SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS

Abstract

Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen for a known disease such as HIV infection are disclosed. The method comprises (a) providing patient information to a computing device (the computer device comprising: a first knowledge base comprising a plurality of different therapeutic treatment regimens for the disease; a second knowledge base comprising a plurality of expert rules for selecting a therapeutic treatment regimen for the disease; and a third knowledge base comprising advisory information useful for the treatment of a patient with different constituents of the different therapeutic treatment regimens; and (b) generating in the computing device a listing (preferably a ranked listing) of therapeutic treatment regimens for the patient; and (c) generating in the computing device advisory information for one or more treatment regimens in the listing based on the patient information and the expert rules.

657040 2025360

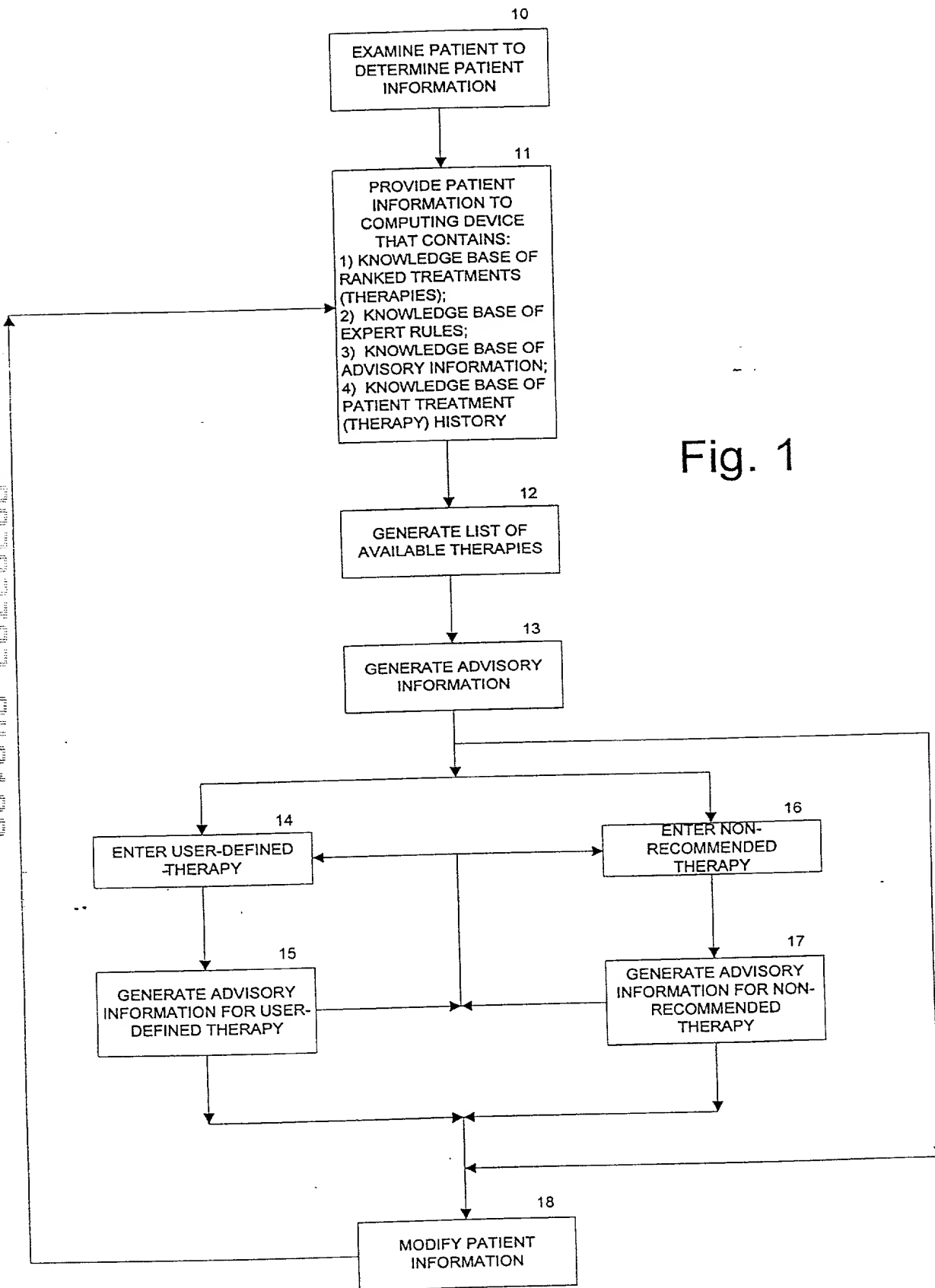


Fig. 1

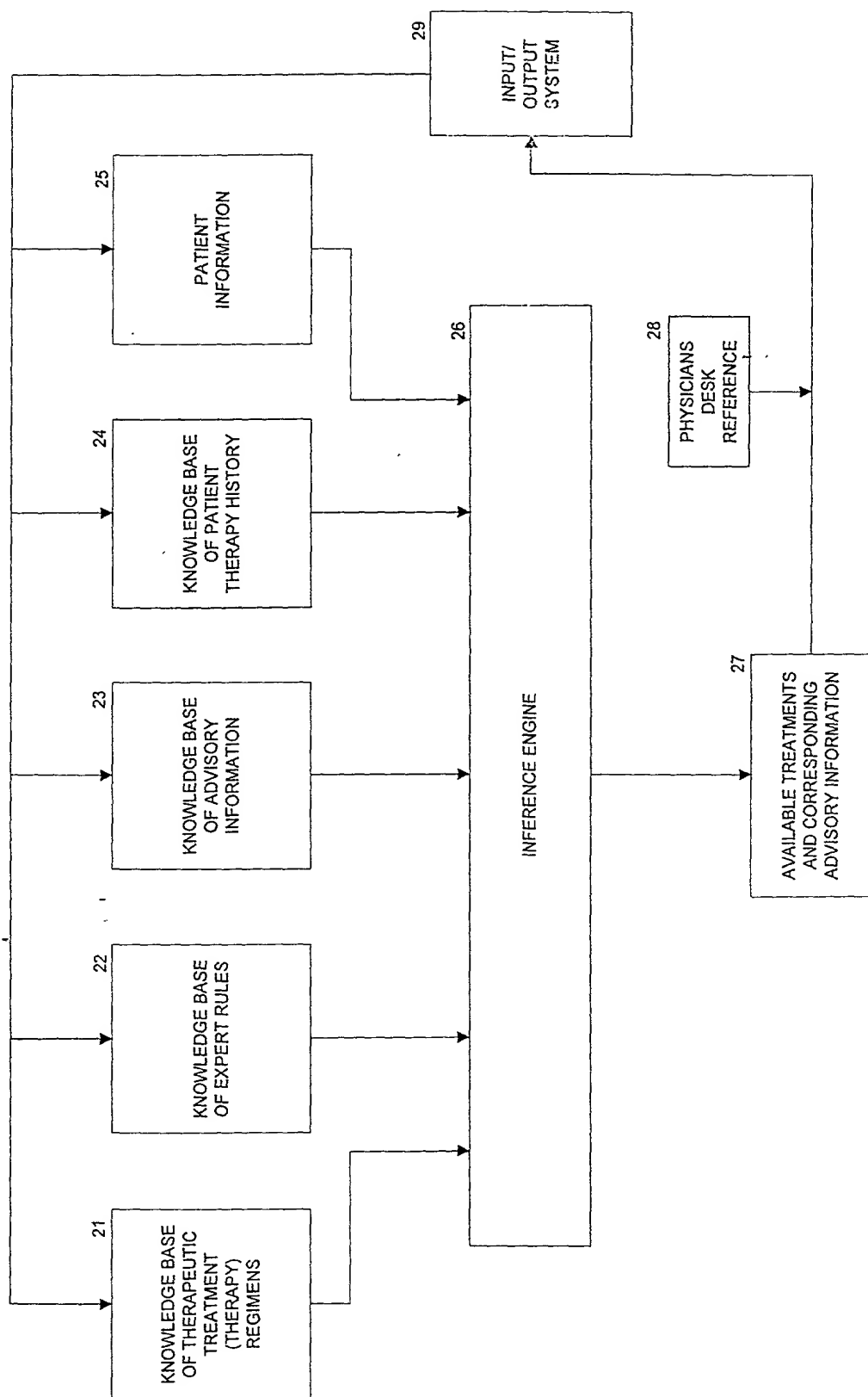


Fig. 2

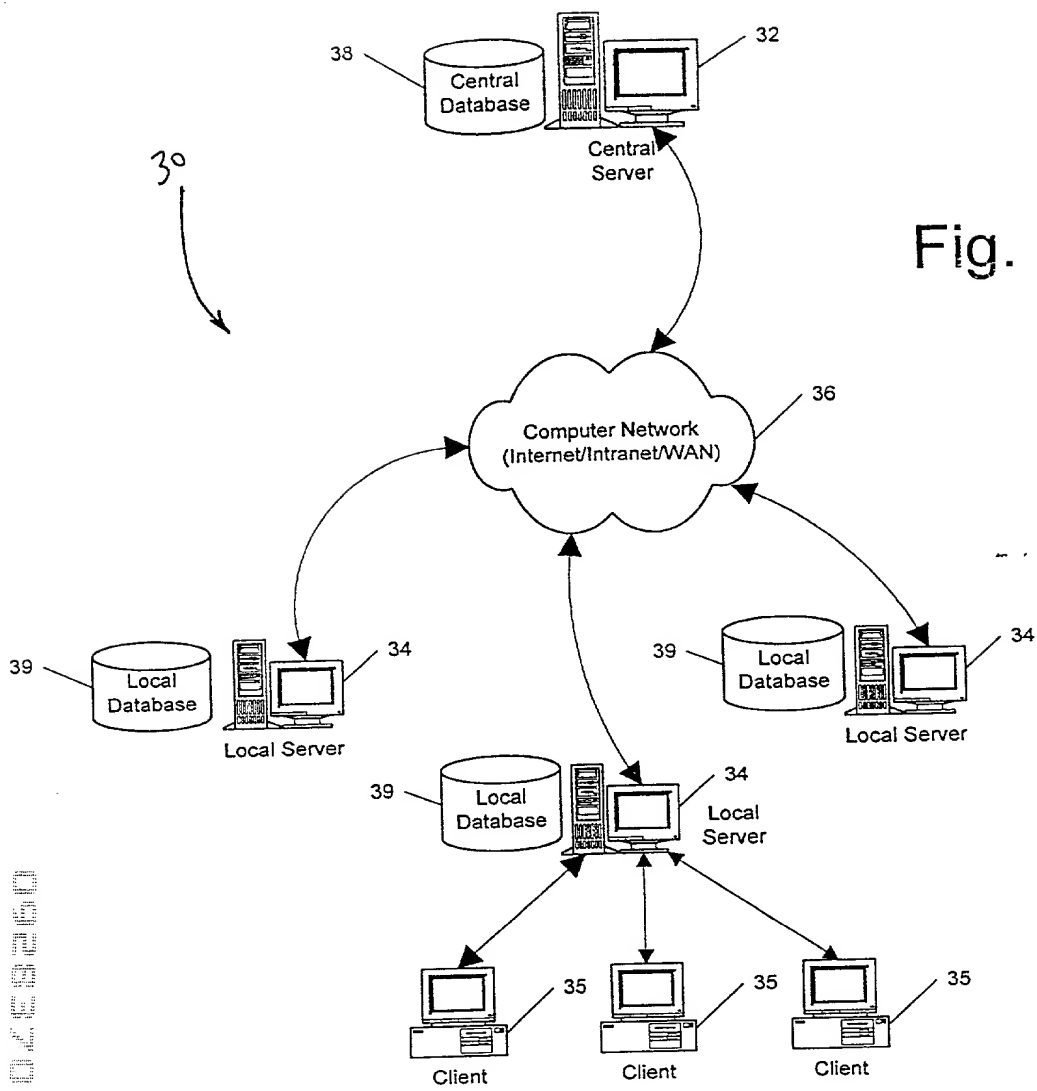
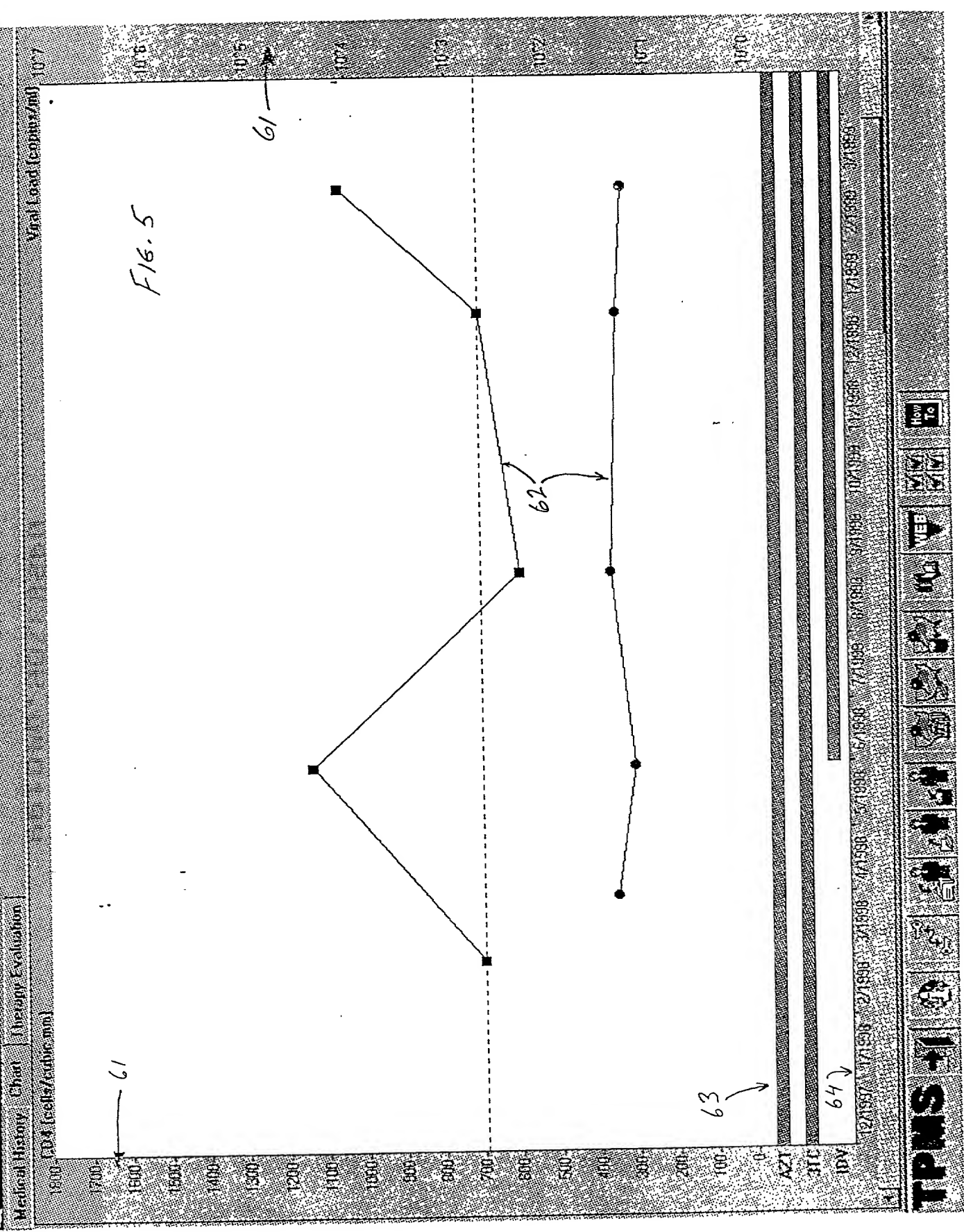


Fig. 3

664040 20250606

F16.4

F16.4



Therapy	EF	Ad	Safety Considerations	Med	Dug	Freq	PI	Cost
△ ddi, d4T, NFV	2	2	ddI Renal dos. Adj, d4T Renal dos. adj	Y		q8h	15	\$30.38
△ ddi, d4T, IDV	3	6	ddI Renal dos. Adj, d4T Renal dos. adj, IDV Renal d...	Y		q8h	12	\$26.80
△ ddi, d4T, RTV	4	7	ddI Renal dos. Adj, d4T Renal dos. adj	Y		q12h	18	\$34.06
△ d4T, SQV-SGC, NFV	5	8	d4T Renal dos. adj	Y		q8h	29	\$45.60
● ddi, SQV-SGC, NFV	5	8	ddI Renal dos. Adj			q8h	31	\$42.24
△ ddC, SQV-SGC, NFV	5	8	ddC Renal dos. adj, tobramycin+ddC		Y	q8h	29	\$42.72
△ ddC, d4T, NFV	8	8	ddC Renal dos. adj, d4T Renal dos. adj, tobramycin+	Y	Y	q8h	13	\$30.86
△ ddi, d4T, SQV-SGC	6	9	ddI Renal dos. Adj, d4T Renal dos. adj	Y		q8h	24	\$31.24

See Also: Top 10 Full Patient Evaluation

Therapy Being d4T, d4T, IDV

Evaluated

Recommended Dosages

- Vilex 125mg q12h (4 pills/day, \$4.22/day)
- Zerit 15mg q12h (2 pills/day, \$7.58/day)
- Crivian 800mg q8h (6 pills/day, \$15.00/day)

(● indicates adjusted dosage)








Warning - Resistance Notices

- d4T: Resistance Advisory : Cross Resistance: The patient has at least one previous exposure to AZT that was greater than one year in duration. Previous AZT exposure can lessen the antiRetroviral effect of d4T due to cross resistance. Therapies containing d4T have been ranked lower in their Adjusted Score by +3.

FullRankB, Commentary259

- Resistance Advisory: IDV: According to the last genotype data entered, the patient's virus currently has the following secondary mutation(s), Q101[P], L54V[P], and I84V[P] which is/are associated with resistance to IDV. These mutations alone are not enough to preclude the use of IDV but they do indicate a trend in this direction. IDV is still an option but ongoing IDV use may result in a more rapid emergence of complete resistance. The Adjusted Score of IDV has been lowered by +3.

F16.7

Icon	Meaning
	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box.
	Indicates that there were no critical alerts for the therapy, however, general warnings and advisories should be read in the Therapy Details box. The book indicates that therapy has been studied and a reference is available to review.
	Indicates a yellow alert. There is important information about this therapy that must be reviewed.
	Indicates a yellow alert. There is important information about this therapy that must be reviewed. The book indicates that therapy has been studied and a reference is available to review.
	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this therapy to be considered.
	Indicates a red alert, which means critical and possible life-threatening situation may exist or may be created with this therapy. Information in the Therapy Details section must be read for this therapy to be considered. The book indicates that therapy has been studied and a reference is available to review.
	Indicates the therapy is not recommended.

739.

09083702-04099

70

76

Therapy Options

Therapy	Eff	Adj	Safety
1 d4T, 3TC, IDV	1	1	
1 AZT, 3TC, IDV	1	1	
1 d4T, 3TC, NFV	1	1	
1 AZT, 3TC, NFV			
1 d4T, 3TC, Zalcitabine			
1 AZT, 3TC, Zalcitabine			
1 ddI, d4T, 3TC			
1 d4T, 3TC, Zalcitabine			
1 d4T, 3TC, Zalcitabine			

TherapyB
Evaluated

General

- Vi
- Me

Show Abstract for Retrovir

Show Abstract for Epivir

Show Abstract for Viracept

Show Therapy Study

Print Details for AZT 3TC NFV

Print Top 10 Therapy Option Details

Hide Column "Eff"

Hide Column "Adj"

Hide Column "Safety Considerations"

Show Column "Med"

Show Column "Drug"

Hide Column "Freq"

Hide Column "Pills"

Hide Column "Cost"

90

FIG. 9

Therapy	Eff	Adj	Safety Considerations	Freq	Pills	Cost
<input checked="" type="checkbox"/> AZT, d4T, NVP	2	2	ddl Renal dos Adj, d4T Renal dos Adj	q8h	15	\$30.38
<input type="checkbox"/> AZT, d4T, RTV	4	4	ddl Renal dos Adj, d4T Renal dos Adj	q12h	18	\$34.06
<input type="checkbox"/> NVP, ABC, EFV	5	5	NVP Renal dos Adj, EFV+Renal Dysf	q12h	9	\$44.32
<input type="checkbox"/> DLV, ABC, EFV	5	5	EFV+Renal Dysf	q8h	19	\$43.21
<input type="checkbox"/> NVP, ABC, EFV	5	5	EFV+Renal Dysf	q8h	16	\$54.40
<input type="checkbox"/> NVP, NVP, EFV	5	5	NVP Renal dos Adj, EFV+Renal Dysf	q8h	17	\$46.41

See More | Yes All | 100% | Full Screen Evaluation

Therapy Being Evaluated: AZT, 3TC, IDV

CAUTION

YELLOW ALERT

CAUTION

• AZT: Medical Condition Alert: This patient has a history of anemia. Use Retrovir with caution due to risk of hematologic toxicity. More Info 171

FullRankC, Commentary 171

73



Recommended Dosages

- Retrovir 300mg q12h (2 pills/day, \$9.56/day)
- Epivir 150mg q24h (1 pill/day, \$3.84/day)
- Crivian 800mg q8h (6 pills/day, \$15.00/day)

(★ indicates adjusted dosage)

Warning - Resistance Notices

- Resistance Advisory: Retrovir and Epivir ranked lower (+2) due to historical virological failure. More Info 364 FullRankC, Commentary 364
- Dolutraic Resistance Advisory: Dolutraic ranked lower (+2) due to historical virological failure. More Info 251

Fig. 108

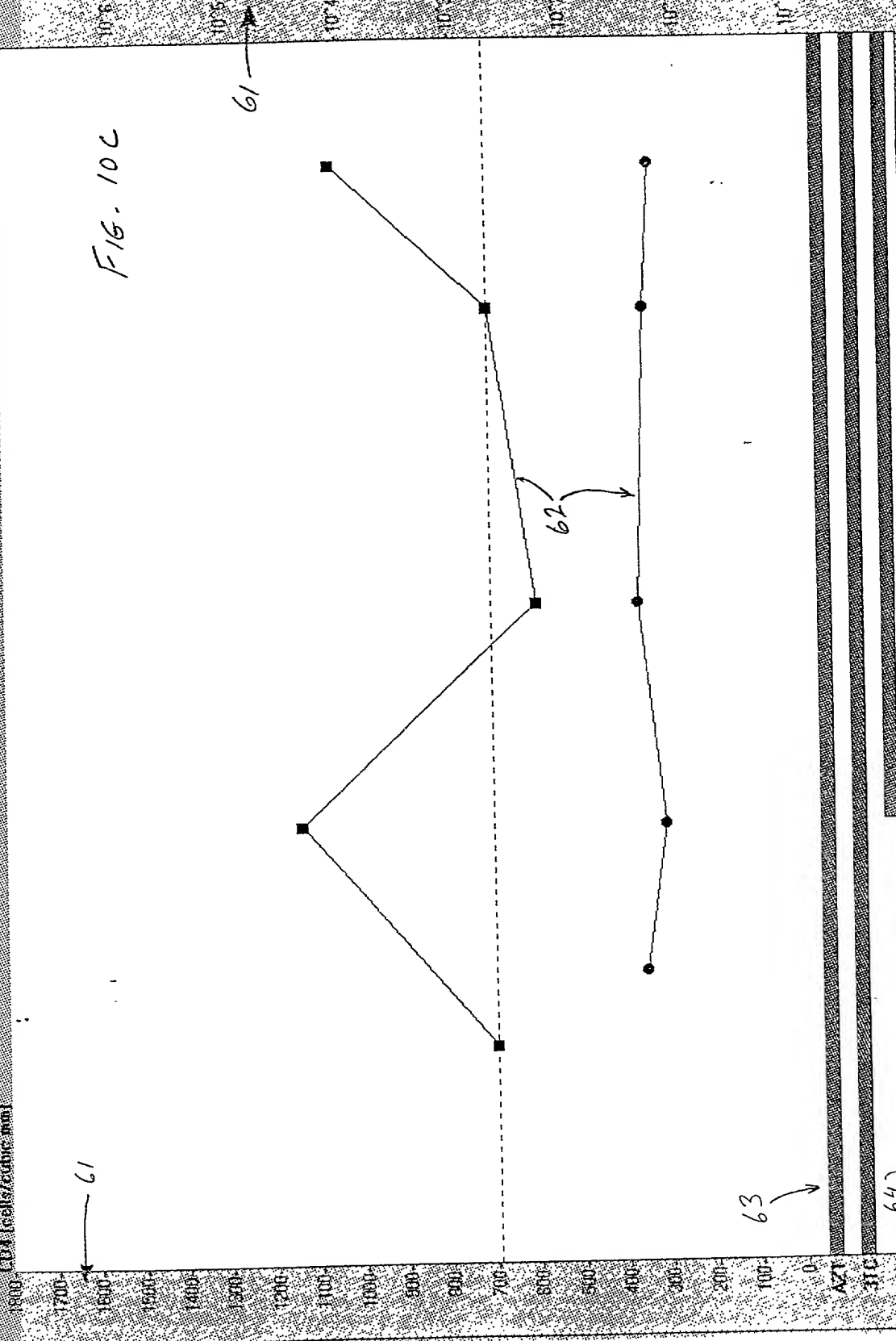
670

60a

70a

Viral Load (copies/mL) 10⁻⁷

FIG. 10C



61

62

63

64

MB1

TPMS Patient

Medical History | Chart | Therapy Evaluation

General

Patient for demo

Birth Date

1/1/1960

TPMS Number

Empty

Weight (kg)

55.00

Date

3/3/1999

Gender

Male

Solid Doseage

Yes

Find

Save

CD4 and Viral Load

CD4 (cells/mm³)

1

3/

Current Viral Load

+

3/

Previous Viral Load

17

HIV Genotype

Phenotype

Allergy/Hypersensitivity

Intolerance

Hemoglobin

Specimen Date

3/1/1999

12

Neutrophils

Specimen Date

3/1/1999

15

Hepatic Function

Specimen Date

3/1/1999

49

Boundry and Prequalification Messages

Please be aware that the following hourly and prequalification conditions currently apply to this patient.

- **Poor Viral Suppression** Δ: The patient's viral load count either did not decrease ≥ 5 log from the last point or is not below the viral load reduction goal. Unless lab errors at fault, consider changing therapy. More Info PQ1 PwQualM6, Commentary445
- **No Baseline Viral Load Value**: Please specify which viral load value or values (an average of two points) you wish to be set as the baseline viral load value for this patient. BOUNDZY, Commentary411a

Data Needed Soon - Caution

OK

Cancel

TPMS +1

How To

50

General		Patient ID: ARV naive		Birth Date: 1/5/1968		TPMS Number:		Weight (kg):		Date: 2/1/1999		Value: 73.00																																																									
Physician:		Gender: Male		Ethnicity:		Solid Dose:		Date: 2/1/1999		Value: Yes																																																											
<table border="1"> <tr> <td colspan="2">CD4 and Viral Load</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">CD4 (cells/mm³)</td> <td colspan="2">2/20/1999</td> <td colspan="2">350</td> <td colspan="2">2/22/1999</td> <td colspan="2">975</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Current Viral Load</td> <td colspan="2">2/20/1999</td> <td colspan="2">31000</td> <td colspan="2">Viral Load</td> <td colspan="2">E/mL</td> <td colspan="2">Viral Load</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Previous Viral Load</td> <td colspan="2">12/29/1998</td> <td colspan="2">19000</td> <td colspan="2">Viral Load</td> <td colspan="2">E/mL</td> <td colspan="2">Viral Load</td> <td colspan="2">2/1/1999</td> </tr> </table>														CD4 and Viral Load		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		CD4 (cells/mm ³)		2/20/1999		350		2/22/1999		975		ALT/AST/ALP		2/1/1999		Current Viral Load		2/20/1999		31000		Viral Load		E/mL		Viral Load		2/1/1999		Previous Viral Load		12/29/1998		19000		Viral Load		E/mL		Viral Load		2/1/1999	
CD4 and Viral Load		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
CD4 (cells/mm ³)		2/20/1999		350		2/22/1999		975		ALT/AST/ALP		2/1/1999																																																									
Current Viral Load		2/20/1999		31000		Viral Load		E/mL		Viral Load		2/1/1999																																																									
Previous Viral Load		12/29/1998		19000		Viral Load		E/mL		Viral Load		2/1/1999																																																									
<table border="1"> <tr> <td colspan="2">HIV Genotype</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">Phenotype</td> <td colspan="2">2/1/1999</td> <td colspan="2">12.50</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Allergy/Hypersensitivity</td> <td colspan="2">2/1/1999</td> <td colspan="2">1350</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Intolerance</td> <td colspan="2">2/1/1999</td> <td colspan="2">1350</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> </table>														HIV Genotype		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		Phenotype		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999		Allergy/Hypersensitivity		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999		Intolerance		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999	
HIV Genotype		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
Phenotype		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
Allergy/Hypersensitivity		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
Intolerance		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
<table border="1"> <tr> <td colspan="2">Hemoglobin</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">Neutrophils</td> <td colspan="2">2/1/1999</td> <td colspan="2">12.50</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Neutrophils</td> <td colspan="2">2/1/1999</td> <td colspan="2">1350</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> </table>														Hemoglobin		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		Neutrophils		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999		Neutrophils		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999															
Hemoglobin		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
Neutrophils		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
Neutrophils		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
<table border="1"> <tr> <td colspan="2">Hepatic Function</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">Renal Function</td> <td colspan="2">2/1/1999</td> <td colspan="2">35</td> <td colspan="2">2/1/1999</td> <td colspan="2">35</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Bilirubin</td> <td colspan="2">2/1/1999</td> <td colspan="2">1.00</td> <td colspan="2">2/1/1999</td> <td colspan="2">1.00</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> </table>														Hepatic Function		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		Renal Function		2/1/1999		35		2/1/1999		35		ALT/AST/ALP		2/1/1999		Bilirubin		2/1/1999		1.00		2/1/1999		1.00		ALT/AST/ALP		2/1/1999															
Hepatic Function		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
Renal Function		2/1/1999		35		2/1/1999		35		ALT/AST/ALP		2/1/1999																																																									
Bilirubin		2/1/1999		1.00		2/1/1999		1.00		ALT/AST/ALP		2/1/1999																																																									
<table border="1"> <tr> <td colspan="2">Current ARV Therapy</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">Non-ARV Drugs</td> <td colspan="2">2/1/1999</td> <td colspan="2">12.50</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> <tr> <td colspan="2">Therapy Drug</td> <td colspan="2">2/1/1999</td> <td colspan="2">1350</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> </table>														Current ARV Therapy		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		Non-ARV Drugs		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999		Therapy Drug		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999															
Current ARV Therapy		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
Non-ARV Drugs		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
Therapy Drug		2/1/1999		1350		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									
<table border="1"> <tr> <td colspan="2">Prozac Pulvules & Liquid, O...</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">Specimen Date</td> <td colspan="2">Value</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">Date</td> </tr> <tr> <td colspan="2">Bactrim DS Tablets</td> <td colspan="2">2/1/1999</td> <td colspan="2">12.50</td> <td colspan="2">2/1/1999</td> <td colspan="2">No</td> <td colspan="2">ALT/AST/ALP</td> <td colspan="2">2/1/1999</td> </tr> </table>														Prozac Pulvules & Liquid, O...		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date		Bactrim DS Tablets		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999																													
Prozac Pulvules & Liquid, O...		Specimen Date		Value		Specimen Date		Value		ALT/AST/ALP		Date																																																									
Bactrim DS Tablets		2/1/1999		12.50		2/1/1999		No		ALT/AST/ALP		2/1/1999																																																									

Fig. 11A

70a

Medical History

Chart

Therapy Evaluation

General

Patient (id) ARV naive1

Birth Date 1/5/1968

Gender Male

TPMS Number

Weight (kg)

Height

Date 2/1/1999

Value 73.00

Physician

Save

Print

Export Paper

OK

Cancel

CD4 and Viral Load

CD4

Cells (cd4/mm)

Current Viral Load

Previous Viral Load

27

27

12

HIV Genotype

Phenotype

Adverse/History

Intolerance

Hemoglobin

Neutrophils

Hepatic Function

Specimen Date

Specimen Date

Specimen Date

Specimen Date

Specimen Date

Specimen Date

12

12

13

13

35

Boundry and Prequalification Messages

Please be aware that the following boundry and prequalification conditions currently apply to this patient

- Therapy Initiation: Current treatment guidelines recommend initiation of antiRetroviral therapy for HIV-infected patients with HIV RNA (viral load) concentrations greater than 20,000 copies/ml (10,000 E_q/ml bDNA) or CD4 counts less than 500 cells/ μ L (Ann. Int. Med., 1998). PreQualM, Commentary61
- Combination Therapy Recommended: Experts agree that the goal of antiRetroviral therapy should be to reduce the viral load to as low a level as possible for as long as possible. Initiation of therapy with a combination containing 2 nucleoside reverse transcriptase inhibitors (NRTIs) and a potent protease inhibitor have been shown to provide enhanced clinical benefit versus 2 drug combinations with regard to reduction in viral load and improved clinical outcomes. PreQualM, Commentary66

OK

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1

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F16-113

MBZ

Therapy Report: AZT, ddI, HIV DLV
Evaluated

Use as Current Therapy

Show Therapies



Recommended Dosages

- Retrovir 300mg q12h (2 pills/day, \$9.56/day)
- Videx 200mg q12h (4 pills/day, \$6.78/day)
- Norvir 600mg q12h (12 pills/day, \$22.26/day)
- Rescriptor 400mg q8h (12 pills/day, \$7.39/day)

Fig. 11D

- AZT: Interrupt Retrovir use if anemia and/or neutropenia develops. More Info 036 DosGenA, Commentary36
- ddI: When treatment with other drugs known to cause pancreatic toxicity is required (for example, IV pentamidine), suspension of Videx should be considered. CmtGenA, Commentary13
- ddI: If patients develop symptoms of neuropathy, Videx therapy should be interrupted. DosGenB, Commentary40
- ddI: Clinical signs suggestive of pancreatitis should prompt dose suspension of Videx and careful evaluation of the possibility of pancreatitis. Only after pancreatitis has been ruled out should dosing be resumed. DosGenB, Commentary30
- DLV: Skin rash attributable to Rescriptor may occur during first 21 days. More Info 034 CmtGenS, Commentary54

- ddI: Videx should not be administered with a prescription antibiotic containing any form of tetracycline. CmtGenA, Commentary15
- ddI: Plasma concentrations of some quinolone antibiotics are decreased when administered with antacids containing magnesium or aluminum. Therefore, doses of quinolone antibiotics should not be administered within 2 hours of taking Videx. CmtGenA, Commentary16
- RTV: Monitor for decreased AUC of Norvir and associated adverse events when concomitant with use of drugs that increase CYP3A activity (including tobacco). More Info 026 CmtGenH, Commentary26

Therapy Options (10 of 613)

Therapy	Eff	Ad	Safety	Contraindications
<input checked="" type="radio"/> AZT, ddI, 3TC, SQV/SGC	1	1	1	1
<input type="radio"/> ddI, 3TC, NVP				
<input type="radio"/> AZT, 3TC, IDV				
<input type="radio"/> AZT, 3TC, NVP				
<input type="radio"/> ddI, 3TC, IDV				
<input type="radio"/> AZT, ddI, RTV, DLV				
<input type="radio"/> ddI, ddI, IDV, NVP				
<input type="radio"/> ddI, 3TC, RTV				
<input type="radio"/> AZT, ddI, RTV, NVP				

See More

Show Abstract for Retrovir

Show Abstract for Virex

Show Abstract for Epivir

Show Abstract for Fuzilease

Show Therapy Study

Print Details for AZT, ddI, 3TC, SQV/SGC

Print Top 10 Therapy Option Details

Print All Therapy Option Summaries

Print Top 10 Therapy Option Summaries

Therapy Being Evaluated

None

WARNING:

CmtGenY, Conf

- Viral Load Testing required: Viral load testing should be repeated 21-35 days after initiation of, or a change of, anti-retroviral therapy to evaluate therapeutic efficacy and patient compliance. CmtGenY, Commentary65

CmtGenY, Conf

Hide Column: Eff

Hide Column: Ad

Hide Column: Safety Contraindications

Show Column: Med

Show Column: Drug

Hide Column: Form

Hide Column: Price

Hide Column: Cost

Show 1 Drug Therapies Show 2 Drug Therapies Show 3 Drug Therapies Show 4 Drug Therapies Show 5 Drug Therapies Show 6 Drug Therapies Show 7 Drug Therapies Show 8 Drug Therapies Show 9 Drug Therapies Show 10 Drug Therapies

Antiretroviral Drugs

Nucleoside Analogues (NRTI)

☐ AZT (Retrovir/zidovudine)

☐ ddI (Videx/ddanosine)

☐ ddC (Hivid/zalcitabine)

☐ 3TC (Epivir/lamivudine)

☐ d4T (Zerit/stavudine)

☐ ABC (Ziagen/abacavir)

Protease Inhibitors (PI)

☐ IDV (Crixivan/indinavir)

☐ SQV-HFSC (Invirase/saquinavir)

☐ SQV-VFSC (Fortovase/saquinavir)

At regimen, the complete product information for each therapeutic component should be consulted

Fig-11E

- Therapy Initiation: Current treatment guidelines recommend initiation of anti-retroviral therapy for HIV-infected patients with HIV RNA (viral load) concentrations greater than 20,000 copies/ml (10,000 E_q/ml bDNA) or CD4 counts less than 500 cells/ μ L (Ann. Int. Med., 1998). PeQualM, Commentary61
- Combination Therapy Recommended: Experts agree that the goal of anti-retroviral therapy should be to reduce the viral load to as low a level as possible for as long as possible. Initiation of therapy with a combination containing 2 nucleoside reverse transcriptase inhibitors (NRTIs) and a potent protease inhibitor have been shown to provide enhanced clinical benefit versus 2 drug combinations with regard to reduction in viral load and improved clinical outcomes. PeQualM, Commentary66

660

TPMS Patient 604 709

Medical History Chart Therapy Evaluation

CD4 (cells/cubic mm)

Viral Load (copies/ml)

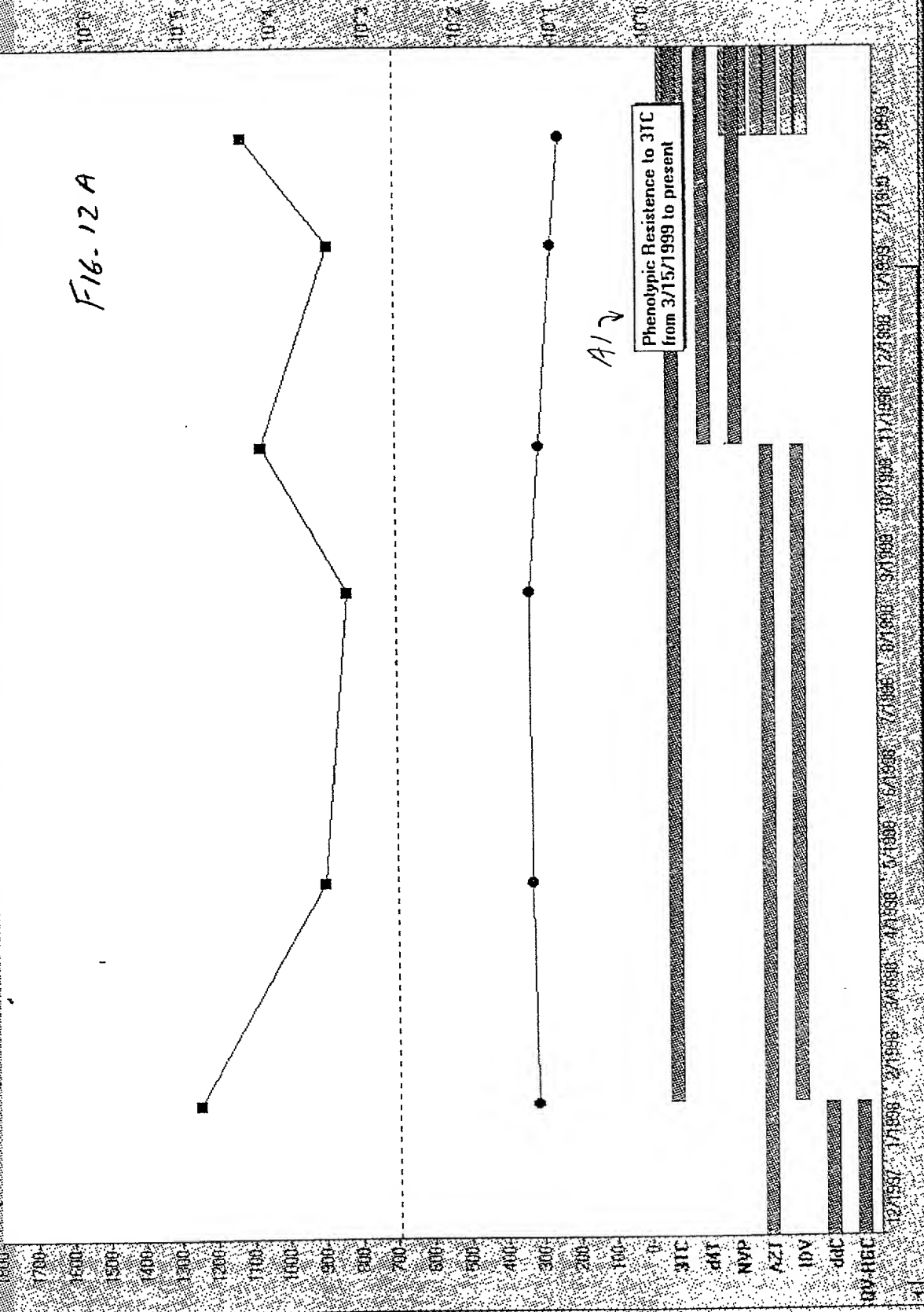


FIG. 12 A

A12

Phenotypic Resistance to 3TC from 3/15/1999 to present

TPMS +1

Navigation icons: Home, Back, Forward, Stop, Print, Find, Web, Mail, etc.

Evaluate Current Therapy: 3TC, d4T, NVP

Therapy Details (19 of 24)

Therapy	EL	Ad	Study Comparisons	Freq	Fill	Cost
1 d4T, d4T, NFV	2	2	Rifabutin+NFV	q8h	15	\$33.88
2 d4T, d4T, EFV	5	5		q12h	9	\$28.44
3 d4T, NFV, EFV	5	5	Rifabutin+NFV	q8h	16	\$38.50
4 d4T, NFV, EFV	5	5	Rifabutin+NFV	q8h	14	\$40.24
5 d4T, NFV, EFV	5	7	Rifabutin+NFV	q8h	15	\$38.77
6 d4T, d4T, EFV	5	7		q8h	8	\$28.71

See More | See All | 100% Full Screen Evaluation

Therapy Being Evaluated: 3TC, d4T, NVP

Evolution

Use of Current Therapy



III THERAPY REJECTED !!!



This therapy was rejected for the following reason(s): Additional information about the therapy is provided but this therapy is NOT advisable

- Viramune (niraparine/NVP) Resistance Advisory: According to the last genotype data entered, the patient's virus currently has mutation(s) which is/are associated with resistance to Viramune. FilMunE, Rejection54
- Resistance Advisory: According to the last genotype data entered, the patient's virus currently has the following mutations, M184V [RT]. The genotype test displays evidence of the M184V/M184I mutation which is associated with resistance to 3TC. However, this mutant has increased sensitivity to the antiRetroviral activity of AZT and ADV so an AZT/3TC or AZT/ADV combination is still useable. Therefore combinations which contain AZT/3TC and AZT/ADV are shown as therapy options although these therapies have been ranked down +5 in favor of three drug combinations with no resistant mutants. FilMunB, Rejection51
- Epir and Viramune Resistance Advisory: The patient's last phenotypic assay demonstrates phenotypic resistance to Epir and Viramune, therefore, therapies containing Epir and Viramune are not recommended at this time. FilResC, Rejection42

F16-123



CAUTION

YELLOW ALERT

CAUTION



LW3

- NVP△: Drug Interaction Alert: Patient is currently taking ifabutin and there is insufficient data to assess whether dose adjustments are necessary. These drugs

TPMS -1



New

General Patient Features1 Birth Date: 1/1/1960 TPMS Number: 1728/1999 Weight (kg): 60.00 Date: 1/28/1999

Physician: patient Gender: Male Child: Save Solid Biopsy: 1/28/1999 Value: Yes

CD4 and Viral Load

CD4 (cells/mm ³)	Specimen Date	Value	Specimen Date	Prev Value
240	3/15/1999	240	1/28/1999	240
Current Viral Load	3/15/1999	21500	C/mL	
Previous Viral Load	1/28/1999	2000	C/mL	

HIV Genotype: H 3/15/1999 L101P, M46[P], I54V[P], V82A[P], M41L[R], Y181

• NVPΔ Drug Interaction Alert Patient is currently taking rifabutin and there is insufficient data to assess whether dose adjustments are necessary. These drugs should only be used in combination if clearly indicated and with careful monitoring. - CmiDIP, Commentary 33

Non-APV Drugs

Drug	Specimen Date	Value	Specimen Date	Prev Value
Hemoglobin	1/28/1999	15.00	1/28/1999	No
Neutrophils	1/28/1999	1500	1/28/1999	No

Hepatic Function

Specimen Date	AST/SGOT (IU/L)	ALT/SGPT (IU/L)	Specimen Date	Panel Function
1/28/1999	25	25	1/28/1999	No

Diagnosis: No Specimen Date: 1/28/1999

End Creatinine: 1.00

End Creatinine: 1.04.17

Fig-12C

DECLARATION AND POWER OF ATTORNEY FOR PATENT APPLICATION

Attorney Docket No. 9045-2

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **SYSTEMS, METHODS AND COMPUTER PROGRAM PRODUCTS FOR GUIDING THE SELECTION OF THERAPEUTIC TREATMENT REGIMENS,**

the specification of which

☒ is attached hereto

OR

☐ was filed on _____ as United States Application No. or PCT International Application Number _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States of America, listed below and have also identified below any foreign application for patent or inventor's certificate, or of any PCT International application having a filing date before that of the application on which priority is claimed.

None			<input type="checkbox"/> Yes <input type="checkbox"/> No
Number	Country	MM/DD/YYYY Filed	Priority Claimed

			<input type="checkbox"/> Yes <input type="checkbox"/> No
Number	Country	MM/DD/YYYY Filed	Priority Claimed

			<input type="checkbox"/> Yes <input type="checkbox"/> No
Number	Country	MM/DD/YYYY Filed	Priority Claimed

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

None	
Application Number(s)	Filing Date (MM/DD/YYYY)

Application Number(s)	Filing Date (MM/DD/YYYY)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) or § 365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application(s) in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application (37 C.F.R. § 1.63(d)).

None		
Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned

Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned

Appln. Serial No.	Filing Date	Status Patented/Pending/Abandoned

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following registered attorney(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

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